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Study Affirms New Therapeutic Target for Malignant Gliomas

The proteasome inhibitor bortezomib (Velcade) kills malignant glioma cells and can enhance the ability of tamoxifen to do the same, NCI researchers reported last week at the American Association of Cancer Research (AACR) annual meeting in Washington, D.C. The findings, the researchers said, lend further support to the rationale behind a phase II clinical trial launched nearly 1 year ago that is testing bortezomib and tamoxifen in patients with recurrent, high-grade malignant gliomas.

Glioma cells appear to always be on the verge of death, and NF-κB appears to play an essential role in keeping them alive.

There has been little progress in the treatment of gliomas, the most common type of brain cancer, over the past two decades; the median survival for those with the most aggressive and most common glioma, glioblastoma, is a little more than a year. Tamoxifen, a selective estrogen receptor modulator, or SERM, is primarily used to treat or prevent breast cancer in women at high risk for the disease. During the last 10 to 15 years, however, tamoxifen also has been a last option *(continued on page 2)*

Director's Update

Guest Update by Dr. John E. Niederhuber

Cancer Control Month: A Message of Hope

President George W. Bush proclaimed April as National Cancer Control Month to "encourage citizens, government agencies, private businesses, nonprofit organizations, and other interested groups to join in activities that will increase awareness of how to prevent and control cancer." The President's official proclamation gave recognition to the goal of increasing public awareness and encouraging people to help themselves prevent certain types of cancer. He urged individuals to take a number of proven steps to reduce their risk, such as avoiding tobacco, eating well, and exercising regularly. In addition, he encourages "all Americans to get regular preventive screenings and speak with a health care provider about additional ways to reduce the risk of developing cancer."

President Bush also praised the federal agencies that have helped the United States "lead the world in cutting-edge medical research." He noted that the Administration's FY 2007 budget request includes $5.9 billion for cancer-related activities by agencies of the U.S. Department of Health and Human Services (HHS)—most of which is through NCI. He promised that "America will continue to *(continued on page 2)*

(Gliomas continued from page 1)
after standard treatments have failed in some glioma patients, said Dr. Howard Fine, of NCI's Center for Cancer Research, and has demonstrated a clinical benefit in some patients.

The current phase II trial, being conducted at the NIH Clinical Center, follows a series of studies conducted in Dr. Fine's lab over several years in which researchers have demonstrated the important role of the intracellular protein NF-κB in glioma cell survival, and that inhibition of NF-κB could enhance the glioma cell-killing activity of tamoxifen and at least one other investigational SERM.

Although tamoxifen induces breast cancer cell death by inhibiting the estrogen receptor, studies by Dr. Fine's lab and others have shown that it kills glioma cells even though those cells do not express the estrogen receptor.

In the study results presented at AACR, NF-κB was highly active in glioma cell lines but never in normal tissue, explained the study's leader, Dr. Ai-Min Hui. And gene-expression profiles on 203 glioma clinical samples revealed that other genes activated by NF-κB were upregulated, which was not the case in healthy samples.

Glioma cells appear intrinsically to always be on the verge of death, Dr. Fine added, and NF-κB seems to play an essential role in keeping them alive, acting like a full-time security system.

"The glioma tumor cells are not just turning NF-κB on in response to stress," he said. "They have this pathway overexpressed all of the time to be able to resist any stress, including chemotherapy or radiation therapy. It's probably one of the reasons gliomas are so resistant to treatment."

Dr. Fine's lab started testing bortezomib, which is approved for use in patients with multiple myeloma, because it's been shown to inhibit NF-κB. The proteasome is a large conglomeration of proteins, known as a complex, inside cells that is responsible for breaking down damaged or unneeded proteins. Bortezomib promotes cancer cell death by disrupting this essential regulatory process which, as a welcome side effect, disrupts NF-κB expression.

In this new study, Dr. Hui explained, they determined that bortezomib's ability to disrupt NF-κB is actually achieved by blocking the activity of another protein that regulates NF-κB's function, IκB-alpha.

Dr. Fine's lab also has found that bortezomib can enhance the cell-killing activity of radiation and chemotherapy.

In addition to the phase II trial at the NIH Clinical Center, the NCI-funded New Approaches to Brain Tumor Therapy Consortium is conducting a phase I/II trial testing bortezomib alone in patients with malignant gliomas for whom standard therapies have failed.

By Carmen Phillips

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aggressively fight cancer, encourage innovative research, and spread hope to those affected."

We share the optimism of the proclamation that the new understanding of diseases, better diagnostic tools, and innovative treatments help provide hope and healing to those who have been diagnosed with cancer.

This message of hope is heard loud and clear in a new series airing on public radio stations this month called "Walking Through the Storm." The four-part series from Human Media and The Networks, Inc., funded by NCI, demonstrates what cancer survivors can teach all of us about hope and the quality of life when faced with a serious illness.

The first hour-long documentary in the series, "Journey for Recovery," recounts how cancer patients confront their fears, real and imagined, and provides a scientific look at how attitude affects health, such as how mind/body techniques can diminsh cancer pain. In the second program, "Humor and Health," professional comedians who are cancer survivors teach the health benefits of humor and laughter. This documentary also interviews playwrights who have used the stage for humor and poignant insight about their journeys through illness.

I hope you will listen in on this inspiring series, and I recommend that you check with your local public radio stations for their scheduling of "Walking Through the Storm."

In addition, NCI's Division of Cancer Control and Population Sciences (DCCPS)—which aims to reduce risk, incidence, and deaths from cancer, as well as enhance the quality of life for cancer survivors—has produced an excellent 12-minute video on "The Excitement of Cancer Control Research," which is available online and well worth your viewing during our April celebration of cancer control. DCCPS conducts and supports an integrated program of the highest quality genetic, epidemiologic, behavioral, social, and surveillance cancer research.

Finally, as we observe National Cancer Control Month, I join President Bush in commending the strength and courage of more than 10 million cancer survivors whose perseverance is an inspiration to all Americans. As he promises, "Cancer can be prevented, treated, and defeated," and we will continue to strive to control the suffering and death due to cancer. ◆

Spotlight

Using Gene Signatures to Discover Cancer Drugs

One of the more common experiments in cancer research is profiling the activity of genes in tumor cells. This reveals patterns of gene activity that can be used to search for potential drug targets.

But rarely has this approach led to a therapy. All too often, it seems, efforts are derailed because identifying a potential drug target from a tumor's genetic signature is difficult, expensive, and time consuming.

A team of researchers addressed this problem 2 years ago by developing a strategy that, in effect, skips the hard part. Rather than dissecting the signature, they suggest, use the signature as a tool for discovering cancer drugs.

"We asked whether a genetic signature itself could be the basis for screening drugs," Dr. Todd Golub of the Dana-Farber Cancer Institute said last week at the AACR annual meeting.

The idea is to identify drugs that can alter the entire genetic program of a cancer cell, allowing the cell to acquire the traits of a normal counterpart. So far, the strategy has apparently worked as planned.

Last year, the researchers used it to discover that gefitinib (Iressa) might be a potential treatment for acute myeloid leukemia (AML). A clinical trial is under way to test the drug in patients with relapsed or refractory cases of AML.

AML was the test case for the signature-based screen because patients with this disease have few treatment options. AML is too rare to attract the attention of most pharmaceutical companies, and new sources of potential drug targets are needed.

"The problem very often in trying to develop drugs is that we don't know the identity of the critical targets" for developing therapies, says Dr. Kimberly Stegmaier, who studies AML at Dana-Farber and helped create the screen.

But with the signature-based screen, no prior knowledge about the biology of the disease is needed. All that's required is the genetic signature of the biological state one is hoping to achieve.

A major problem in AML is that certain cells do not mature, or differentiate, into normal blood cells. Thus, Dr. Stegmaier identified a signature associated with differentiation and then screened for chemicals that could induce the signature in AML cells.

The screen included many FDA-approved drugs to increase the chances of finding new uses for drugs known to be safe. This could lead quickly to a clinical trial.

"One of the goals from the start has been to translate discoveries in the lab rapidly into clinical medicine," says Dr. Stegmaier.

The screen yielded a candidate, but the chemical had been abandoned in development and never turned into a drug. The researchers knew, however, that the chemical inhibits the epidermal growth factor receptor (*EGFR*) gene.

Dr. Stegmaier then screened another *EGFR* inhibitor, gefitinib, using cells from eight patients recently diagnosed with AML. Gefitinib induced differentiation in the majority of the samples.

Based largely on these results and the fact that 100,000 lung cancer patients have taken gefitinib safely, the researchers launched the clinical trial. By year's end, they expect to have 20 individuals enrolled in the phase II study.

Dr. Stegmaier cautions that it is still early and the drug might not be as effective in patients as it was in the laboratory.

An important question not necessarily answered by the screening strategy is: Why is a drug effective?

In the case of AML, the researchers do not yet know. They do know that in cells from AML patients, gefitinib is not hitting the target it had been developed for, *EGFR*. This gene is not even turned on in AML.

"Ironically, this is not how the drug works," says Dr. Stegmaier, noting that several recent studies have described the off-target effects of targeted therapies.

The researchers say they are working hard to identify the true target or targets of gefitinib in AML cells because this might allow them to develop more potent drugs.

"Clearly there are additional targets to be characterized," Dr. Golub said

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Cancer Research Highlights

Secondhand Smoke Linked to Decreased Lung Cancer Survival

Lung cancer patients who had been exposed to high levels of secondhand smoke over many years did not live as long on average as patients who had been exposed to lower levels, researchers reported last week at the AACR annual meeting. The study, led by Dr. David Christiani of Harvard Medical School, might be the first to show a strong association between exposures to secondhand smoke and survival in patients with lung cancer.

The study included 393 patients diagnosed with early-stage, non-small-cell lung cancers (NSCLCs) at Massachusetts General Hospital and followed them for 5 years. At diagnosis, patients provided information on their exposures to secondhand smoke in the home, at work, and at places of leisure, such as restaurants. For the analysis, patients were divided into quartiles based on their average exposure levels.

The highest quartile had more than 48 years of exposure; those in the lowest had on average less than 28 years of exposure. Patients with the least exposure had the highest survival rates, and the overall 5-year survival rate decreased with increasing exposure: 71 percent of patients with the lowest exposure were alive after 5 years, while just 47 percent of those with the highest exposure survived 5 years.

The association between secondhand smoke and survival in lung cancer patients was strong even after taking into account age, gender, stage of cancer, and the patients' cigarette smoking habits over their respective lifetimes (of the group, 37 percent were current smokers, and 8 percent were never smokers). The most important factor appeared to be workplace exposure, perhaps because of the amount of time people spend at work and/or the higher levels of secondhand smoke they might be exposed to there.

"The take-home message is that people should try their best to limit their exposure to secondhand smoke," said Dr. Wei Zhou of the Harvard School of Public Health, who presented the results.

Study Points to Potential Method for Overcoming Trastuzumab Resistance

The inability of some women with HER2-positive breast cancer to clinically respond to treatment with trastuzumab (Herceptin) may be overcome by combining the drug with an agent that inhibits PI3K, an intracellular growth-promoting protein. Researchers from the University of Texas M.D. Anderson Cancer Center, led by Dr. Dihua Yu, a professor in the Department of Surgical Oncology, reported lasted week at the AACR annual meeting that they tested seven different PI3K inhibitors and found that two of them, when combined with trastuzumab, increased its antitumor activity in a breast cancer mouse model.

The study builds on previously published work by Dr. Yu and colleagues, in which women who failed to respond to trastuzumab had tumors with low levels of *PTEN*, a known tumor-suppressor gene.

Because *PTEN* exerts its tumor-suppressor function in part by inhibiting PI3K, the group decided to test some PI3K inhibitors in clinical development to see if they could mimic the effect that *PTEN* would have if it were being expressed at adequate levels. Two of these agents showed antitumor activity when combined with trastuzumab, triciribine, and RAD001 (everolimus). The latter combination, Dr. Yu said, had an additive therapeutic effect on tumor growth in a mouse model of breast cancer compared with trastuzumab alone.

"We think the combination of Herceptin and a PI3K inhibitor is affecting multiple cancer pathways," Dr. Yu said. "It will be interesting to see if other PI3K inhibiting agents now being developed also will work in HER2-positive, *PTEN*-negative tumors, as well as in other breast tumors that lack *PTEN*."

M.D. Anderson is launching a phase I/II trial to test the combination of RAD001 and trastuzumab in women with HER2-positive breast cancer who have failed to respond to trastuzumab alone as a first-line therapy.

Nicotine May Interfere with Lung Cancer Chemotherapy

A new study from investigators at the H. Lee Moffitt Cancer Center and Research Institute, University of South Florida, published online April 6 in the *Proceedings of the National Academy of Sciences* has shown that nicotine has the potential to interfere with the activity of several chemotherapy drugs commonly used to

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(Highlights continued from page 4)
treat NSCLC. This research highlights the importance of smoking cessation for lung cancer patients, but also raises the possibility that nicotine replacement products that help patients quit smoking—such as nicotine patches—may also interfere with cancer treatment.

When the investigators treated NSCLC cell lines with gemcitabine, cisplatin, or paclitaxel in the presence of nicotine, the apoptotic (cell-killing) effects of all three chemotherapy drugs were suppressed. Molecular analysis revealed that this suppression was mediated by increased levels of the proteins survivin and x-linked inhibitor of apoptosis (XIAP). These two antiapoptotic proteins interact with specific subunits of the nicotinic acetylcholine receptors, which are found on the surface of lung cancer cells. When both survivin and XIAP were targeted with small interfering RNAs, the antiapoptotic effect of nicotine was reversed and the cells were again sensitive to the chemotherapy drugs.

In light of these results, the investigators stress the need to take the effects of nicotine into account in the development of new treatments for lung cancer.

Study Suggests Significant Social Value of Cancer Mortality Reduction

The social value of a 1-percent reduction in U.S. cancer mortality would be approximately $500 billion, according to a new study by economists from the University of Chicago.

Speaking last week at the AACR annual meeting, study co-author Dr. Kevin Murphy, who was recently named a MacArthur Fellow, argued that the study results suggest that, even if it had only a one-in-five chance of reducing mortality, it would be "worthwhile" to spend an additional $100 billion on cancer research.

To conduct the study, the authors developed a complex framework that placed a value on health improvements, such as new life-extending treatments for heart disease or cancer. This framework was based, he explained, on assessments of Americans' willingness to pay for improvements in longevity. The researchers then used the framework to estimate the value of individual financial gains seen as a result of advances in public health over the past three decades and to place a social value on future gains.

They found, for example, that the gains in life expectancy seen during the last three decades of the 20th century added nearly $3.2 trillion annually in national wealth. And while a permanent 1-percent mortality reduction would have a social value of approximately $500 billion, a cure for cancer would be worth approximately $50 trillion, they concluded.

The study did not directly account for the value of improved quality of life, Dr. Murphy noted, or factors such as increased productivity.

The danger, he stressed, is that gains in longevity and health brought about by a substantial increase in cancer research (and other areas of biomedical research) could be offset by costs associated with delivering the interventions generated by this research.

"Cost containment," Dr. Murphy concluded, "is an essential component of arguing for increased research funding."

Genes May Play Role in Lung Cancers of Never Smokers

Genetic factors may help explain why some people who have never smoked develop lung cancer, researchers reported last week at the AACR annual meeting. Their evidence comes from a comparison showing that first-degree relatives (parents, siblings, and children) of lung cancer patients who never smoked were 25 percent more likely to develop any type of cancer than the relatives of a comparison group of healthy individuals. The cancers diagnosed in the relatives include colorectal, melanoma, head and neck, lung, prostate, and breast.

In one of the largest such studies to date, Dr. Margaret Spitz of the University of Texas M.D. Anderson Cancer Center and her colleagues determined the incidence of cancer in 2,465 first-degree relatives of 316 lung cancer patients who never smoked. For comparison, they determined the incidence rate of cancer in 2,442 first-degree relatives of 318 healthy individuals.

The relatives of lung cancer patients had more than a sixfold increased risk of developing lung cancer than relatives in the comparison group. The cancer group also had a 44-percent excess risk of developing cancer before age 50 than the comparison group; relatives in the cancer group were on average 10 years younger at the time of diagnosis than relatives in the comparison group who developed cancer.

"We suspect that genetic susceptibility plays a role in lung cancer in patients who have never smoked," said Dr. Olga Gorlova of M.D. Anderson, who presented the findings. "Our next step is to prove that there is a genetic component in this risk." Among the genes she plans to study are those involved in repairing damage to DNA. ◆

Legislative Update

NIH Budget Heard in the House

On April 6, the House of Representatives Subcommittee on Labor, HHS, and Education held a hearing on the NIH FY 2007 budget. NIH Director Dr. Elias Zerhouni, who presented testimony before the committee, was accompanied by leadership from several NIH institutes, including NCI Deputy Director Dr. John Niederhuber.

Most committee members expressed concerns over the terms of the FY 2007 budget proposal and how it will, if adopted, impact the progress of scientific research.

In his oral testimony, Dr. Zerhouni discussed some of NIH's accomplishments since the doubling of the NIH budget from 1998 to 2003.

"Discoveries fueled by this investment are transforming the practice of medicine," Dr. Zerhouni said. "We can now clearly envision an era when the treatment paradigm of medicine will increasingly become more predictive, personalized, and preemptive."

One such example, Dr. Zerhouni explained, is a new test under development for women with breast cancer that uses gene expression profiles to predict whether some patients with breast cancer will benefit from, and thus should receive, chemotherapy. He also highlighted a recent report that, for the first time in seven decades, showed that the absolute number of annual cancer deaths has fallen.

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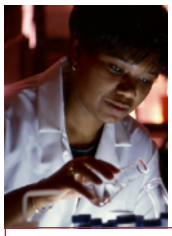

Featured Clinical Trial

MRI-Guided Radiotherapy for Prostate Cancer

Name of the Trial
Phase I Study of MRI-Guided Intensity-Modulated External-Beam Radiotherapy in Patients with Prostate Cancer (NCI-05-C-0191). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-05-C-0191.

Principal Investigator
Dr. Anurag Singh, NCI Center for Cancer Research

Dr. Anurag Singh

Why This Trial Is Important
An estimated 234,460 American men will be diagnosed with prostate cancer in 2006. Many of these men will undergo external-beam radiation therapy to treat their cancer.

In this study, doctors will use a new method called intensity-modulated external-beam radiation therapy (IMRT) to treat men with localized prostate cancer. Patients will undergo a magnetic resonance imaging (MRI) procedure, and doctors will use the resulting images to pinpoint areas of the prostate containing cancer cells. The presence of cancer in these areas will be confirmed with biopsies. Doctors will then treat the areas identified as cancerous with higher doses of radiation, while delivering a standard dose of radiation to the rest of the prostate and surrounding normal tissue.

"When treating prostate cancer, higher radiation doses have produced better outcomes," said Dr. Singh. "This trial is an attempt to use IMRT and MRI imaging, confirmed by MRI-guided biopsy, to direct much higher doses of radiation to those areas of the prostate containing tumor cells. The remainder of the prostate will receive standard radiation doses. This may allow us to more effectively treat the tumor without increasing toxicity to normal tissue."

With this phase I trial, researchers will study the side effects and determine the best dose of MRI-guided radiation therapy for treating patients with prostate cancer.

Who Can Join This Trial
Researchers will recruit up to 36 patients aged 18 to 89 with a confirmed diagnosis of prostate adenocarcinoma that has not spread to other parts of the body. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/NCI-05-C-0191.

Study Site and Contact Information
The study is taking place at the NIH Clinical Center in Bethesda, Md. For more information about this trial, call the NCI Clinical Studies Support Center toll free at 1-888-NCI-1937. This call is confidential. ◆

An archive of "Featured Clinical Trial" columns is available at http://cancer.gov/clinicaltrials/ft-all-featured-trials.

Notes

Jianhua Gan Wins SER-CAT Young Investigator Award

Dr. Jianhua Gan, a visiting fellow in the Biomolecular Structure Section, Macromolecular Crystallography Laboratory, has won the 2006 SER-CAT (Southeast Regional Collaborative Access Team) Young Investigator Award. The SER-CAT organization consists of 25 member institutions and was established in 1997 to provide third-generation x-ray capabilities to macromolecular crystallographers and structural biologists in the southeastern region of the United States. The Young Investigator Award, which is designed to recognize the most significant contributions to the scientific program at SER-CAT each year, was presented on March 10 at the annual SER-CAT Symposium in Atlanta. Dr. Gan was recognized for his work on the structural biology of double-stranded RNA processing by ribonuclease III.

INCa-NCI JRPF Program Is Announced

The National Cancer Institute of France (INCa) and NCI have announced a new Joint Research Project Fellowship (JRPF) Program. By training the next generation of cancer researchers together, INCa and NCI aim to foster relationships among cancer researchers in France and the United States. The JRPF Program is open to any aspect of cancer research; however, applications are encouraged for projects involving cancer prevention research, basic research, preclinical/translational research, clinical research, epidemiological research, psychosocial research, behavioral research, and research aimed at improving palliative care and end-of-life care for cancer patients.

It is anticipated that two JRPFs will be awarded in each of the next 3 years. Successful applicants are expected to begin the first leg of the research prior to the end of the current calendar year, will spend 12 to 18 months in each country, and will participate in a joint research project under the mentorship of a French PI and a U.S. PI. Go to http://www.e-cancer.fr and http://www.cancer.gov/oia for more information.

NCI Listens and Learns

Nanotechnology is the creation of microscopic materials used to manipulate matter at an incredibly small scale—between 1 and 100 nanometers, which is about 1/80,000 the width of a human hair. Nanotechnology can be applied in diagnostic imaging by designing injectable, targeted contrast agents that can improve the resolution of cancer imaging to the level of a single cell. Nanotechnology research can be applied to design devices that can be customized to optimally deliver medications for treating conditions, including pain and nausea, and those that can more effectively kill cancer cells.

These are just two examples of how NCI is working to harness the power of nanotechnology to radically change the way cancer is diagnosed, treated, and prevented.

NCI would like feedback from the advocacy community and the public on the following:

- Are cancer patients and others aware that nanotechnology is being used in cancer research?
- Do cancer patients and others think nanotechnology is important for cancer research?

Go to http://ncilistens.cancer.gov to register and post your comments. ◆

(Spotlight continued from page 3)

at AACR. "It's important to find and exploit those additional targets."

He has been asked about the decision to start clinical trials without understanding why a drug might be helping patients. His response is that it's an easy decision when the circumstances warrant it.

"If there is a safe drug, and there are patients in need, then let's move ahead with trials while trying to figure out the mechanism," said Dr. Golub.

By Edward R. Winstead

(Legislative Update continued from page 6)

Dr. Niederhuber had the opportunity to speak about NCI's cancer Biomedical Informatics Grid (caBIG™) and the importance of making crosscutting scientific information available to researchers. Questions concerning NCI's Specialized Programs of Research Excellence program were also addressed. Dr. Niederhuber elaborated on NCI's efforts to fund the best quality of science available and affirmed the institute's commitment to translational research. Both Drs. Zerhouni and Niederhuber touted NCI's role in the development of vaccines against human papillomavirus, the primary cause of cervical cancer worldwide, as an important example of success in preempting disease, with potential to have great international impact. ◆

Featured Meetings and Events

A calendar of scientific meetings and events sponsored by the National Institutes of Health (NIH) is available at http://calendar.nih.gov. ◆

Funding Opportunities

Information Technologies and the Internet in Health Services and Intervention Delivery
Announcement Number: PA-06-224
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R21 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3368. Inquiries: Dr. Audie Atienza—atienzaa@mail.nih.gov

Information Technologies and the Internet in Health Services and Intervention Delivery
Announcement Number: PA-06-225
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R03 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3369. Inquiries: Dr. Audie Atienza—atienzaa@mail.nih.gov

Information Technologies and the Internet in Health Services and Intervention Delivery
Announcement Number: PA-06-226
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R01 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3370. Inquiries: Dr. Audie Atienza—atienzaa@mail.nih.gov

Understanding and Treating Tuberous Sclerosis Complex
Announcement Number: PAS-06-205
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, 2008.

This is a renewal of PAS-05-085 and will use the R03 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3366. Inquiries: Dr. Mary Ellen Perry—mp372j@nih.gov

Understanding and Treating Tuberous Sclerosis Complex
Announcement Number: PAS-06-206
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, 2008.

This is a renewal of PAS-05-085 and will use the R21 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3367. Inquiries: Dr. Mary Ellen Perry—mp372j@nih.gov

Developmental Biology and Regeneration of the Liver
Announcement Number: PA-06-231
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R01 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3371. Inquiries: Dr. John S. Cole III—jc121b@nih.gov; Dr. Asad Umar—au9q@nih.gov

Developmental Biology and Regeneration of the Liver
Announcement Number: PA-06-232
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R21 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3372. Inquiries: Dr. John S. Cole III—jc121b@nih.gov; Dr. Asad Umar—au9q@nih.gov

Research on Social Work Practice and Concepts in Health
Announcement Number: PA-06-233
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R03 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3380. Inquiries: Dr. Suzanne Heurtin-Roberts—sheurtin@mail.nih.gov ◆

The *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads the national effort to eliminate the suffering and death due to cancer. Through basic, clinical, and population-based biomedical research and training, NCI conducts and supports research that will lead to a future in which we can identify the environmental and genetic causes of cancer, prevent cancer before it starts, identify cancers that do develop at the earliest stage, eliminate cancers through innovative treatment interventions, and biologically control those cancers that we cannot eliminate so they become manageable, chronic diseases.

For more information on cancer, call 1-800-4-CANCER or visit http://www.cancer.gov.

NCI Cancer Bulletin staff can be reached at ncicancerbulletin@mail.nih.gov.